

Microbial Trigger for Autoimmunity?

If suffering through a cold or the flu weren't bad enough by itself, a new study hints at the existence of a mechanism by which microbial infections may inflame or even initiate autoimmune disorders such as multiple sclerosis.

Autoimmune disorders are one of the continuing mysteries of immunology. These diseases initially confounded researchers, who thought the immune system deleted all cells capable of acting against the body's own tissues.

In recent years, however, investigators have found that people and animals harbor immune cells that, though normally inactive, can selectively target the body's own molecules.

What spurs these dormant cells into a deadly rebellion? Infections have long been a prime suspect, since they frequently predate the onset of an autoimmune disorder or a worsening of an existing autoimmune illness.

One infection-based theory of autoimmunity, known as molecular mimicry, begins with the observation that some molecules of microorganisms resemble those of the host they infect. Consequently, as the host mounts a defense against infecting microbes, it may inadvertently activate some immune cells that recognize its own molecules.

Several investigators now propose that one of the body's initial responses to infection, the production of a compound called interleukin-12, may also awaken self-reactive immune cells.

"It's a more universal mechanism than that of molecular mimicry," says Benjamin M. Segal of the National Institute of Allergy and Infectious Diseases (NIAID) in Bethesda, Md.

Segal and his colleagues study a mouse disease called experimental allergic encephalomyelitis. It resembles multiple sclerosis in that the animal's immune cells destroy the myelin that surrounds and insulates nerve cells.

In recent studies, the researchers isolated immune cells from a strain of mice resistant to the disease. Some of those cells can target myelin basic protein, a component of myelin, but nonetheless seem to ignore its presence.

When exposed to bacterial DNA or a particular component of bacterial cell walls, the immune cells become activated, Segal and his colleagues report in the June 1 *JOURNAL OF IMMUNOLOGY*. Mammalian DNA provoked no response. Previous investigators had made similar findings and attributed them to repetitive CG nucleotide sequences, which occur frequently in bacterial DNA but rarely in mammalian DNA.

Segal's group further found that severe to moderate autoimmune disease results if the cells that react to myelin basic protein are exposed to bacterial DNA or the cell wall component and are then injected into mice.

More important, the researchers have largely pieced together how these microbial products ignite autoimmunity. Macrophages and other immune cells that are the first to respond to infections react to the bacterial material by producing interleukin-12. This potent immune system stimulator then triggers the production of compounds that help the immune system create an army of cells specific to a particular microbe.

In test-tube studies, the researchers found that this production of interleukin-12 can also arouse the self-reactive immune cells that cause autoimmune problems. In theory, this chemical call to arms against a pathogen may activate immune cells that happen to be near an infection, causing them to turn against the body.

While earlier studies in animals had

shown that bacterial products can induce autoimmunity, the process "has never been analyzed in detail like this," says Charles A. Janeway of Yale University School of Medicine.

"It's a potentially important mechanism," adds David S. Pisetsky of Duke University Medical Center in Durham, N.C. "There's a lot of interest in the interplay between infections and autoimmune diseases and in what impact bacterial and microbial products have."

Very few microbial infections may actually lead to autoimmune diseases, note researchers. "There's probably a lot of mechanisms that dampen autoimmune responses," says study coauthor Ethan Shevach of NIAID.

Shevach and his colleagues suggest that interleukin-12 inhibitors may aid people with autoimmune disorders. Such diseases are particularly difficult to treat because physicians must find ways to dampen the autoimmune attack without severely curtailing normal immune responses. "That's always the tradeoff," says Pisetsky. —J. Travis

Ring up a microscopic light switch

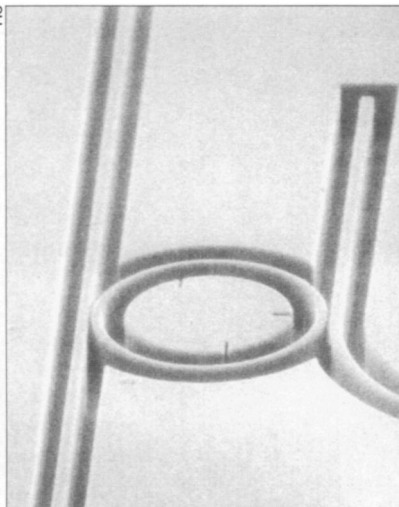
The idea of manipulating photons instead of electrons in microscopic circuits has long appealed to researchers interested in speeding up optical communications and information processing.

Recent advances in the miniaturization of lasers have provided one of the key building blocks of photonic integrated circuits. Now, researchers have fabricated another essential component of such a system—a tiny switch that can channel photons from one path to another.

It's the smallest optical switch yet produced, says electrical engineer Seng-Tiong Ho of Northwestern University in Evanston, Ill. Ho and his coworkers describe their device in a paper accepted for publication in *OPTICS LETTERS*.

Called a microcavity resonator, the device consists of a ring or disk made from layered gallium arsenide and aluminum gallium arsenide. When light of just the right wavelength travels down a narrow waveguide (in effect, a wire for photons) close to the resonator, it leaks into the resonator, where it circulates. The circulating light, in turn, channels into another, nearby waveguide. Light at other wavelengths stays in its original path.

Ho and his colleagues have already constructed a photonic wire laser, in which a microscopic tube squeezes confined photons into a laser beam (SN: 6/10/95, p. 367). By combining resonators with lasers on a chip, researchers can manipulate light to handle communication over optical fibers. Eventually, such components could serve as the basis for an optical computer. —I. Peterson



A narrow gap, 0.1 micrometer (μm) wide, separates a ring, 10.5 μm in diameter, from each of two waveguides. When light of precisely the right wavelength (1555.6 nanometers) travels down the straight waveguide (left), the ring, or resonator, acts as a switch, channeling light into the curved waveguide (right).